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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
SPIEGLER, ALEXANDER H

ART UNIT	PAPER NUMBER
1637	9

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/973,278	FISCHER ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *May 9th, 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1,13,17-21 and 23-70* is/are pending in the application.

4a) Of the above claim(s) *1,13,17-21,23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II (Claims 25-70, the polypeptide encoded by HHTLF25 and SEQ ID NO: 164) in Paper No. 7, filed on May 9th, 2003 is acknowledged. Preliminarily, it is noted, Claims 30, 36, 43, 50, 55, 60 and 65 (drawn to methods of producing a protein), have been included in Group II.

2. Applicants traverse the restriction requirement in paper No. 6. The traversal is on the ground(s) that Groups I-X are directed to subject matter that is closely interrelated and therefore examination of all of the groups would not place an undue burden on the Examiner. This is not found persuasive because it is maintained that undue burden would be required to examine the claims of Groups I-X. Restriction of related inventions is proper if it can be shown that the inventions have a different classification, or have acquired a separate status in the art or have a different field of search (see MPEP 808.02). The claims of groups I-X have acquired a separate status in the art as recognized by their different classification and as recognized by their divergent subject matter. Furthermore, it is maintained that each of the inventions are distinct for the reasons discussed in the previous Office action. A search of the distinct inventions would not be co-extensive as evidenced by the requirement for searching different keywords and by the different classification of each invention. Therefore, undue burden would be required to examine each of the claimed inventions. Accordingly, the requirement is still deemed proper, and is therefore maintained.

3. Currently, Claims 1, 13, 17-21 and 23-70 are pending. Claims 1, 13, 17-21 and 23-24 have been withdrawn as being drawn to a non-elected invention (see MPEP § 821), and Claims 25-70 have been examined on the merits.

Information Disclosure Statement

4. The information disclosure statement of Paper No. 8 complies with CFR 1.97, 1.98, and M.P.E.P. 609, and has been considered (see enclosed signed PTO-1449).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 37-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 37-70 are directed to isolated proteins which are at least 90-95% identical to SEQ ID NO: 164, at least 90-95% identical to amino acid residues 27 to 11 of SEQ ID NO: 164, at least 90-95% identical to the secreted portion (or complete polypeptide) of the polypeptide encoded by the HHTLF25 cDNA contained in ATCC Deposit No. 209125, and contiguous amino acid residues of SEQ ID NO: 164. Claims reciting 90% and 95% sequence identity are inclusive of sequences from other species, mutated sequences, and allelic variants having

different functional activities than that of the protein in SEQ ID NO: 164. Claims drawn to proteins "consisting of at least" (i.e., comprising) any 30 or 50 contiguous amino acid residues of SEQ ID NO: 164, includes a large genus of proteins, having unique functional activities, whereas applicants only disclose one member of the genus (i.e., SEQ ID NO: 164) and haven't disclosed any other proteins having portions of SEQ ID NO: 164. In addition, proteins having any 30 or 50 residues of SEQ ID NO: 164 would be expected to have unique functional activities, wherein the specification has not disclosed any proteins having functional activities different from those of SEQ ID NO: 164. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention. The invention is, for purposes of the written description inquiry, *whatever is now claimed* (See page 1117)." The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (See Vas-Cath at page 1116)."

The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's

were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 25-70 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The specification teaches that Gene 14, which encodes SEQ ID NO: 164, is "expressed primarily in macrophages, and to a lesser extent in primary dendritic cells and neutrophils." (pg. 57, ln. 28 to pg. 59, ln. 12, especially pg. 58, ln. 17-18, and is also reiterated on page 10 of Applicants response of Paper No. 7).

Applicants alleged the following utilities:

- "polypeptides of the invention would be useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunologically mediated disorders." (pg. 58, ln. 19-22);

- "polypeptides would be useful in providing immunological probes for differential identification of the tissue(s) or cell type(s)." (pg. 58, ln. 23-24);

- "polypeptides corresponding to this gene would be useful for the diagnosis, treatment, and/or prevention of immune disorders including: leukemias, lymphomas, auto-immunities, immunodeficiencies (e.g., AIDS), immuno-suppressive conditions (transplantation) and hematopoietic disorders." (pg. 59, ln. 5-8);

- "expression of this gene product in macrophage and primary dendritic cells also strongly indicates a role for this protein in immune function and immune surveillance." (pg. 59, ln. 8-10);

- "the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues".

I. *The specification does not assert a specific utility because the utilities asserted by Applicants are general utilities that would be applicable to broad class of the invention.*

MPEP 2107.01 states:

> A "specific utility" is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. Office personnel should distinguish between situations where an applicant has disclosed a specific use for or application of the invention and situations where the applicant merely indicates that the invention may prove useful without identifying with specificity why it is considered useful. For example, indicating that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. Similarly, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for

> the invention, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. Knapp v. Anderson, 477 F.2d 588, 177 USPQ 688 (CCPA 1973). (MPEP 2107.01)

In the instant case, the alleged utilities are not specific utilities because the specification does not disclose a specific biological activity for SEQ ID NO: 164, and furthermore, the specification fails to reasonably correlate the activity of SEQ ID NO: 164 and a specific disease or condition. For example, Applicants gene assert that SEQ ID NO: 164 would be useful as useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample, immunological probes for differential identification of the tissue(s) or cell type(s), the diagnosis, treatment, and/or prevention of a laundry list of possible diseases, disorders and conditions, and as a tissue marker. These utilities are not specific because they would be applicable to the broad class of the invention, especially in light of the lack of disclosure regarding any correlation between the claimed polypeptide and any disease, disorder or condition.

Applicants have not "disclosed a specific use for or application of the invention and situations", but have instead, "merely indicate[d] that the invention may prove useful without identifying with specificity why it is considered useful." Accordingly, the claimed invention is not supported by a specific utility.

II. *The specification does not assert a substantial utility because the utilities asserted by Applicants requires or constitutes carrying out further research to identify or reasonably confirm a "real world" use.*

MPEP 2107.01 states:

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. For example, ...[a]n assay that measures the presence of a material which has a stated correlation to a predisposition to the onset of a particular disease condition would also define a "real world" context of use in identifying potential candidates for preventive measures or further monitoring.

In the instant case, the alleged utilities summarized above do not define a "real world" use because the claimed polypeptide can only be used for "basic research such as studying the properties of the claimed product itself *or the mechanisms in which the material is involved*", and therefore, the claimed polypeptide can only be used for carrying out further research to identify or reasonably confirm a "real world" context of use. (emphasis added) That is, given Applicant's disclosure, the skilled artisan would still need to experiment to find a correlation between SEQ ID NO: 164 and a particular disease, disorder or condition. The specification only teaches that Gene 14, which encodes SEQ ID NO: 164, is "expressed primarily in macrophages, and to a lesser extent in primary dendritic cells and neutrophils." (pg. 58, ln. 17-18), but does not teach any correlation between expression and specific disease states, for example. Therefore, the specification, at best, provides only a starting point for correlating the activity of SEQ ID NO: 164 and any disease, disorder, or condition. It is apparent that extensive further research, not considered to be routine experimentation, would be required before one skilled in the art would know how to use the claimed invention.

For example, in order for a polypeptide to be useful for diagnosis of a disease, there must be a well-established or disclosed correlation or relationship between the claimed polypeptide and a disease or disorder. The presence of a polypeptide in tissue that is derived from cancer cells is not sufficient for establishing a utility in diagnosis of disease in the absence of some information regarding a correlative or causal relationship between the expression of the gene

encoding the claimed polypeptide and the disease. If a molecule is to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is either present only in cancer tissue to the exclusion of normal tissue or is expressed in higher levels in diseased tissue compared to normal tissue (i.e., overexpression). Evidence of a differential expression might serve as a basis for use of the claimed polypeptide as a diagnostic for a disease. However, in the absence of any disclosed relationship between the gene encoding the claimed polypeptide and any disease or disorder and the lack of any correlation between the claimed polypeptide with any known disease or disorder, any information obtained from an expression profile would only serve as the basis for further research on the observation itself. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ 696 (US SupCt 1966.

Accordingly, because the alleged utilities require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use, the specification does not assert a substantial utility.

III. *The specification is not supported by a well-established utility because one of ordinary skill in the art would not immediately appreciate why the invention is useful based on the characteristics on the invention.*

MPEP 2107 states:

> An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible."

Applicants have provided little to no evidence of the characteristics of the claimed polypeptide, the specification does not assert a specific or substantial utility, and based on the lack of correlation between SEQ ID NO: 164 and any disease, disorder or condition, it is not apparent as to how "a person of ordinary skill in the art would immediately appreciate why the invention is useful". This is evidenced by the fact that further research would need to be carried out by the skilled artisan, even given SEQ ID NO: 164 (see discussion above in II). For these reasons, the specification is not supported by a well-established utility.

Finally, MPEP § 2107 states:

"The 35 U.S.C. 101 and 112 rejections shift the burden of coming forward with evidence to the applicant to:
(i) Explicitly identify a specific and substantial utility for the claimed invention; and
(ii) Provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established **at the time of filing**".

In the instant case, Applicants have not "explicitly identif[ied] a specific and substantial utility for the claimed invention". Furthermore, the specification has not provided any evidence that "one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established **at the time of filing**".

It is noted, in Paper No. 7, Applicants assert that the post-filing date art of Lanier et al., Bakker et al, and Lucas et al., confirm that Applicant's invention is specific and substantial. However, as stated above, Applicant must provide evidence that one of ordinary skill in the art would have recognized that the identified specific and substantial utility was well-established **at the time of filing**. The conclusions made by Lanier, Bakker and Lucas (e.g., overexpression of DAP12 results in sever lymphopenia and inflammation) were not discussed, let alone

contemplated in the instant application, and therefore, Applicants may not rely on post-filing date art to provide evidence of a specific and substantial utility.

Accordingly, the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility.

9. Claims 25-70 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

10. No Claims are allowable. The prior art neither teaches nor suggests SEQ ID NO: 164.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (703) 305-0806. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax numbers for the organization where this application or proceeding is assigned are (703) 308-4556 and (703) 308-4242. Applicant is also invited to contact the TC 1600 Customer Service Hotline at (703) 308-0198.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
July 23, 2003

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
7/24/03